SWEET DELUSION

How Safe Is Your ARTIFICIAL SWEETENER? Part One: The Hidden History of Aspartame

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WARNING:
Side effects may include:
Seizures. Depression. Brain damage.
Memory loss. Migraine headaches.
Numbness. Blindness.

Serious sounding repercussions. Surely the FDA would warn you if it knew a common product might trigger reactions like these.

Not so.

This substance, sweetly packaged, rests quietly on tabletops, in soft drinks, chewing gum, vitamins and in medicines.[37,55] The illusion it portrays is as free of warning as a Sunday stroll in the park.

Consumers recognize it by its attractive red and white swirled logo, and are drawn by its promise of an all-natural, low-calorie, sweet flavor.

In a country obsessed by dieting and abhorrent of the perceived sins of sugar, this product has gained unprecedented popularity since it was discovered accidentally thirty years ago by a chemist mixing chemicals in search of a medicine to relieve ulcers.

NutraSweet. Equal. Equal Measure. Spoonful. Its brand names are ubiquitous in food and food products as it corners the market on low calorie sweeteners. Aspartame, as it is known generically, skyrocketed to its position as the most popular sugar substitute in the world shortly after it gained approval for public consumption.

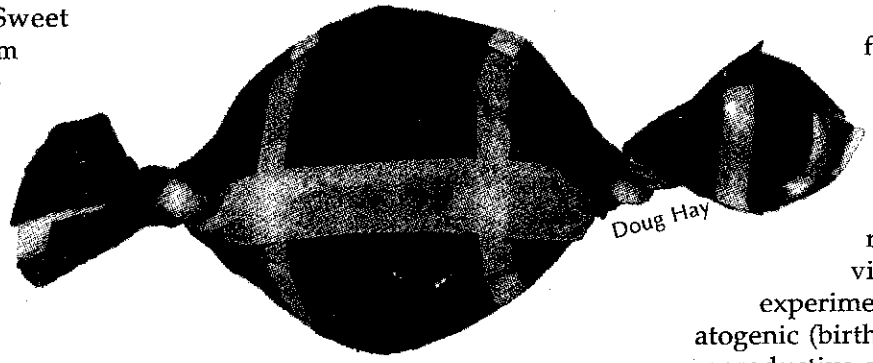
Worldwide, the aspartame industry's sales of the product amount to over $1 billion yearly.[58] In the United States, NutraSweet en-

joys a $700 million sales share, and shows no signs of retreat.[58,68] The NutraSweet group became a part of G.D. Searle Company, a pharmaceutical business, after one of its chemists discovered the sweetener, and realized the sales potential of a sugar substitute. Searle and NutraSweet are now owned by Monsanto Company.

Producers of NutraSweet maintain their platform that the safety of aspartame has been confirmed. They cite affirmation of aspartame by a number of agencies and organizations nationwide, including the American Medical Association, the World Health Organization, the American Academy of Pediatrics, the American Diabetes Association, the American Dietetic Association, and the American Epilepsy Association.

Yet aspartame came amazingly close to not being approved by the Food and Drug Administration (FDA) in the first place. What aspartame actually is, and how it affects certain individuals, is at the heart of a continuing controversy over its increasing distribution in food (including food served in hospitals), medicine, candy, confections, cereal, soft drinks, and scores of other products.

Known chemically as aspartame ($C_{14}H_{18}N_2O_5$), NutraSweet is a compound composed of the following chemicals by weight: methanol (10%), aspartic acid (40%), and phenylalanine (50%). In dry form, the composition is stable, however, when placed in liquid it can break down into its component parts (methanol, aspartate, and phenylalanine). Heat will speed its breakdown. Another breakdown product is diketopiperazine (DKP). In certain combinations these elements can result in adverse reactions in some people. Methanol further breaks down into formaldehyde and formic acid, both known to cause serious side effects in sensitive individuals.[58,64,67,69]



The *Random House Dictionary* defines methanol (also known as methyl alcohol) "as a colorless, poisonous liquid used chiefly as a solvent, fuel, etc."[70]

Methanol is on the Environmental Protection Agency's (EPA) Community Right To Know List, and is reported in EPA's Toxic Substances Control Act Inventory. Sax's Dangerous Properties of Industrial Materials states methanol is "a human poison by ingestion."[71]

The levels of methanol are quite low in a single serving of a product containing aspartame, provided that it has not been exposed to heat or left for a long time on the shelf. Because these factors promote the breakdown of aspartame into its component parts, researchers are concerned that high consumption levels combined with aspartame's unstable shelf life may allow methanol to reach toxic levels in some cases.[21,72]

Human systemic effects from methanol include changes in circulation, cough, headache, nausea and vomiting, optic nerve neuropathy, respiratory effects, and visual field changes. In experiments, it has shown teratogenic (birth defects) and adverse reproductive effects. Genetic mutations from methanol have been reported in human tissue. Methanol is classified as a narcotic.[71]

According to Sax, methanol's "main toxic effect is exerted upon the nervous system, particularly the optic nerve, and possibly the retinae which can progress to permanent blindness. Once absorbed, methanol is only very slowly eliminated. Coma resulting from massive exposures may last as long as 2-4 days. In the body, the products formed by its oxidation are formaldehyde and formic acid, both of which are toxic. Because of the slow elimination, methanol should be regarded as a cumulative poison. Though single exposures to fumes may cause no harmful effect, daily exposure may result in the accumu-

Aspartame TimeLine

December 1965 James Schlatter, G.D. Searle Company chemist, discovers aspartame (NutraSweet, Equal, Spoonful) while testing an anti-ulcer drug. Schlatter said he was "heating aspartame in a flask with methanol when the mixture bumped onto the outside of the flask... some of the powder got onto my fingers... when licking my finger to pick up a piece of paper, I noticed a very strong sweet taste... I felt that this dipeptide was not likely to be toxic."[1]

December 28, 1970 Confidential internal memo at Searle indicates concern over lack of complete toxicological data on diketopiperazine (DKP), an aspartame by-product.[2]

March 5, 1973 Searle petitions the Food and Drug Administration (FDA) for approval of aspartame for use in food.[3]

July 26, 1974 FDA Commissioner Alexander Schmidt, M.D., approves aspartame as a food additive for dry foods only, including chewing gum.[4]

August 1974 Consumer attorney James Turner and Dr. John Olney, Washington University researcher, file objections to FDA's approval of aspartame citing evidence of brain lesions and neuroendocrine disorders in animal studies and concerns that it may cause brain damage and mental retardation in humans. They request a hearing on the safety of aspartame.[5,6]

July 23, 1975 FDA Commissioner Schmidt appoints a task force to investigate Searle's animal studies on aspartame to determine if Searle submitted false information to FDA.[7]

December 5, 1975 Turner and Olney waive their right to a public hearing and agree to a Public Board of Inquiry to hear safety concerns.[8,9]

December 5, 1975 The FDA task force

Continued on next page

lation of sufficient methanol in the body to cause illness. Death from ingestion of less than 30 ml (milliliters) has been reported."[71]

Phenylalanine is an amino acid. However, in high levels it can cause brain damage. People with phenylketonuria are at risk for brain damage if they consume even just one liter of aspartame sweetened soda pop in a day, because the disease inhibits the body's ability to metabolize it.[67,72]

The FDA and the Centers for Disease Control have received nearly 7,000 complaints, including five deaths, attributed to the use of aspartame in food products since the FDA first permitted limited use in 1981.[39,47,56]

A number of researchers and doctors around the country object not only to the product itself, but to the questionable preliminary research that led FDA to approve it for use in dry products in 1981.

Aspartame was the accidental discovery of chemist Jim Schlatter, who was working for Searle on an anti-

Aspartame is unstable in liquids and breaks down into methyl alcohol, a "cumulative poison" which further breaks down into formaldehyde.

ulcer drug. It was December 1965; Schlatter licked his finger and tasted the substance that had spilled on his flask. Its sweetness stunned him, and he realized that tiny amounts of the chemicals he'd been mixing were powerfully sweet.

Searle began testing the chemical mixture — aspartame — and it eventually gained FDA approval, but not without concerns about its safety.

A consumer hotline was organized in 1987 to answer questions about the sweetener and its potential deleterious effects.[74] Doctors and researchers have protested both its use and the research that led to its approval. A number of books have been published denouncing and challenging its self-portrayed description as an innocuous food additive. And victims of its side effects are listed in doctors' case studies.[1,57-66,75,76,79]

After reviewing scientific and medical literature on aspartame published since 1970, Cherry Gaffney of the Armed Forces Institute of Pathology concluded aspartame's ingestion may lead to blood pressure instability and perceptual disorders in some persons. She said that additional studies were necessary to evaluate the impact of aspartame on aviation.[65] Her warning was directed to pilots whose performance could be affected by using the substance.

The organization of the Aspartame Consumer Safety Network in 1987 was the direct result of the founder's nightmarish encounter with aspartame. In 1989 Mary Stoddard related her physical and emotional decline in 1984 during an attempt to lose weight. She said she experienced dozens of symptoms that she'd never had before. She described ringing in her ears, tremors, weakness in her limbs, muscle cramping, twitching, blocked ears, skin lesions, depression, sinus congestion, blurred vision, joint pains, and hearing loss. Stoddard did not have symptoms until she started using diet products, like soft drinks, which contained aspartame. As she continued to use more and more diet products containing aspartame, she observed her symptoms worsened.

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Aspartame timeline continued from page 5

concludes that some of Searle's research practices were so severely flawed that test results were unreliable. Based on this conclusion FDA upholds aspartame approval. The Public Board of Inquiry is delayed.[6,9]

March 24, 1976 The FDA's task force reports, "At the heart of the FDA's regulatory process is its ability to rely upon the integrity of the basic safety data submitted by sponsors of regulated products. Our investigation clearly demonstrates that, in the G.D. Searle Company, we have no basis for such reliance now." The task force further says, "Some of our findings suggest an attitude of disregard for FDA's mission of protection of the public health by selectively reporting the results of studies in a manner which allays the concerns of questions of an FDA reviewer."[10]

July 1976 In response to the task force findings, FDA decides to investigate aspartame studies to determine whether FDA could rely on these studies to assess aspartame's safety.[11]

January 10, 1977 In a 33-page letter, FDA Chief Counsel Richard Merrill recommends to U.S. Attorney Sam Skinner that a grand jury investigate Searle for "apparent violations of the Federal Food, Drug, and Cosmetic Act, 21 U.S.C. 331(e), and the False Reports to the Government Act, 18 U.S.C. 1001, for "their willful and knowing failure to make reports to the Food and Drug Administration required by the Act, 21 U.S.C. 355(i), and for concealing material facts and making false statements in reports of animal studies conducted to establish the safety of (aspartame)." The FDA calls special attention to studies investigating the effect of NutraSweet on monkeys and hamsters.[12]

January 26, 1977 Searle's law firm, Sidley and Austin, request a meeting with Skinner prior to the submission of

Stoddard did not initially link aspartame to her symptoms. She believed that a healthy diet and regular exercise would make her feel physically better, but she continued to have health problems that had no apparent source. She said that she sought medical help, but received conflicting advice. She said she eventually began to suspect the products containing aspartame in her diet were creating her problems after she traced the onset of the symptoms to aspartame use, and on that hunch she decided to eliminate NutraSweet from her diet.

She began to feel better immediately after removing the products containing aspartame from her diet, but Stoddard said it took six months for the symptoms to completely recede. At one point during her recovery she inadvertently ingested a food product containing aspartame, and had a recurrence of the symptoms. She then had no doubt that aspartame was the root cause of her unusual reactions.

In 1987, three years after her own adverse reactions to NutraSweet, Stoddard formed the Aspartame Consumer Safety Network to help others afflicted with aspartame sensitivity problems.

Some specialists in food and nutrition have spoken out against aspartame use. Woodrow Monte, R.D., Ph.D., director of the Arizona State University Food Sciences and Nutrition Laboratory, is uncomfortable with the methanol content of aspartame. In a 1986 interview, Monte called aspartame "a crime against humanity."

"Humans are 100 times more sensitive to methanol than animals. When you ingest aspartame, it breaks down into methanol within one hour of ingestion. Methanol forms as soon as aspartame goes into solution and increases the longer it is in solution," according to Monte.

Because heat speeds the breakdown of aspartame into methanol, if aspartame is added to coffee or tea at 80° C (145° F), one half of the amount breaks down into methanol in 10 minutes, according to Monte. This raises serious concern about aspartame's 1993 approval for use in baked goods and other heated products, like hot cocoa and tea.

"Humans are 100 times more sensitive to methyl alcohol than animals. When you ingest aspartame, it breaks down into methyl alcohol within one hour."

Although aspartame came about as the result of a search for a drug, and its compounds were the basis for a potential prescription medication, the petition for approval of NutraSweet was based on the premise that it was a food additive. The FDA followed its precedent of permitting manufacturers to conduct their own product safety research.

Monte feels that aspartame was mislabeled from the beginning. "Aspartame is a drug, not a food additive," he said. "One hundred million people, from little babies to the elderly, are consuming this stuff in megadoses, more than they ever would if it were labeled a drug."

Dr. Jacqueline Verrett, a former FDA toxicologist, and member of an FDA task force that investigated the authenticity of research done by Searle to establish the safety of aspartame, says she believes the original aspartame studies were "built on a foundation of sand."[20]

She testified in front of a U.S. Senate hearing in 1987 that flawed tests conducted by Searle — used as the basis of FDA approval — were a "disaster" and should have been "thrown out." She said she believed the studies left many unanswered questions about possible birth defects and the safety of aspartame.[20]

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Verrett said the team was instructed not to be concerned

any matters relating to Searle to a grand jury.[13]

February 2, 1977 Skinner is offered a job with Sidley and Austin.[7]

March 8, 1977 Skinner sends a confidential memo citing his preliminary employment discussions with the law firm of Sidley and Austin. He states it would be inappropriate for him to make any decision on the Searle investigation. He says a decision on the grand jury investigation should wait until a new U.S. attorney is appointed. (Note: The statutes of limitation on any prosecution against Searle regarding violations of the Food, Drug and Cosmetic Act regarding aspartame would expire for the monkey study on October 10, and on December 8, 1977 for the hamster study.)[14]

April 13, 1977 A Justice Department memo advises Skinner to proceed with the grand jury investigation as soon as possible, citing the statute of limitations deadline.[15]

July 1, 1977 Skinner leaves his post with U.S. Attorney General's office and joins Searle's law firm, Sidley and Austin.[7]

August 1977 The Bressler Report, compiled by FDA investigators and headed by Jerome Bressler, is released. The report found that 98 of the 196 animals died during one of Searle's studies and weren't autopsied until later dates, in some cases over one year after they died. Records for approximately 30 animals showed substantial differences between original observations on pathology sheets and the observations on pathology sheets submitted to the FDA. There were numerous other inconsistencies and errors noted. For example, a rat was reported alive, then dead, then alive, then dead again; a mass, a uterine polyp, and ovarian neoplasms were found in animals but not reported or diagnosed in Searle's reports. The FDA investigators found dose-related uterine polyps in 15% of 34 animals.[16]

August 1977 Aspartame is dropped from the Department of Justice investi-

Continued on next page

with, or comment upon, the overall validity of the study. She said a subsequent review discarded or ignored the problems and deficiencies outlined by her team's original report. She said, "serious departures from acceptable toxicological protocols" that her investigative team noted in the reevaluation of these studies were also discounted.[20]

She warned that any of the improper practices would compromise

A former FDA toxicologist testified the studies used to approve aspartame were a "disaster" and "should have been thrown out."

and negate a safety study of a food additive. Verrett concluded the data in the study was worthless, and the safety of aspartame and its breakdown products have therefore not been determined.[20]

She emphasized that aspartame exists in the marketplace without basic toxicity information. She said there are no data to assess the interactions with DKP, excess phenylalanine, other aspartame metabolites, additives, drugs, or other chemicals.

In her testimony, Verrett elaborated on DKP problems, including significant increases of uterine polyps and changes in blood cholesterol. DKP is formed when liquids in particular are pre-sweetened with aspartame. The production of DKP is vulnerable to increase in temperature, and higher temperatures produce increasing amounts of DKP. She reminded members of the Congressional Committee "that is why initially, aspartame was not intended or not planned to be used in liquids because of this decomposition ... it was decided it was too unstable to be used in hot preparations, hot liquids, and also in diet drinks."[20]

Senator Howard Metzenbaum (D-OH), chairman of the hearing when Verrett testified, asked her if she disagreed with FDA's position that tests for aspartame safety were credible. Verrett succinctly said she disagreed.[20]

Dr. H. J. Roberts, a Florida internist and author, cites case studies of individuals adversely affected by aspartame use.[75] In one case described by Roberts, the destruction left in the wake of aspartame use was so debilitating that a college honor student deteriorated from the brain damage and finally had to be institutionalized because her mental retardation was so severe.

Roberts said he treated the 18-year-old student in 1986 because of "profound intellectual deterioration" that followed her use of aspartame products for weight control.

The young woman suffered mental incapacitation that destroyed her academic goal when she had a drop of 20 I.Q. points, according to Roberts, who said prior to use of the aspartame she had been an outstanding student at a major university, as well as a skilled typist and pianist.

Her skills had rapidly declined, according to Roberts, by the time of her first visit to his office. Her physical complaints included headaches, decreasing vision in one eye, dizziness, intense drowsiness, tremors, insomnia, suicidal depression, itching, burning on urination, personality change, abdominal pain, recurrent nausea, loss of menstrual cycle, and an ironic 15-pound weight gain.

Roberts said extensive neurophysical tests were conducted on the

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gation of Searle.[7]

September 28, 1977 The FDA's Bureau of Foods Task Force reports that the studies concerning aspartame conducted by Searle "appear to be authentic." H.R. Roberts, the primary recipient of this paradoxical document, subsequently left the FDA and became the vice president of the U.S. National Soft Drink Association.[7,18,19]

October 10, 1977 The statute of limitations expires on Searle's longitudinal study of the effects of aspartame on monkeys which showed seizures in some primates that were never autopsied.[7]

December 8, 1977 The statute of limitations expires on the study of aspartame toxicity in hamsters.[7]

March 1979 The FDA's Center for Food Safety and Nutrition concludes that the deficiencies noted in the reviews by the FDA and by the Universities Associated for Research and Education in Pathology, Inc. were not significant enough to invalidate Searle's aspartame studies. The FDA decides to convene a Public Board of Inquiry.[11]

June 1, 1979 The FDA establishes a Public Board of Inquiry to rule on safety issues surrounding NutraSweet.[21]

January 15, 1980 The Public Board of Inquiry holds hearings on objections to aspartame approval.[6,22]

September 30, 1980 The Public Board of Inquiry concludes NutraSweet should not be approved pending further investigations of brain tumors in animals. The board states it "has not been presented with proof of reasonable certainty that aspartame is safe for use as a food additive."[6,8,23,24]

March 1981 An FDA commissioner's panel is established to review issues raised by the Public Board of Inquiry.[11]

May 19, 1981 Three of six in-house FDA scientists, Dr. Robert Condon, Dr. Satya Dubey, and Dr. Douglas Park, advise

woman, and no consistent patterns were found for a primary disorder or schizophrenia.

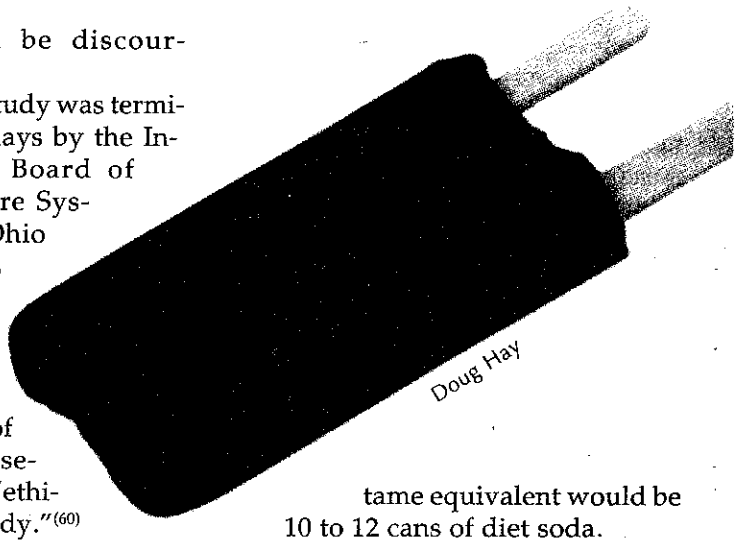
When he noted the woman experienced drowsiness after ingesting aspartame drinks and dozed while driving, he advised her to avoid aspartame, and to follow an anti-

One study was terminated after only 20 days because the reactions among the patients with a history of depression were so severe they could not "ethically continue the study."

hypoglycemic diet with medication. Avoidance of aspartame relieved her symptoms, but the apparent brain damage remained, requiring her placement in a facility for the mentally retarded.[75]

In a recent study investigating the consequences of aspartame on people with mood disorders, Ralph Walton M.D., Robert Hudak, Ph.D., and Ruth J. Green-Waite concluded "individuals with mood disorders are particularly sensitive to this artificial sweetener (aspartame) and its use in this population should be discouraged."[60]

Walton said their study was terminated after only 20 days by the Institutional Review Board of Western Reserve Care System, Youngstown, Ohio because the reactions (including a detached retina and a conjunctival hemorrhage) among the patients with a history of depression were so severe they could not "ethically continue the study."[60]



The study included a total of 13 subjects. Eight of the subjects were patients, ranging in age from 24 to 60 years. All suffered from recurrent major depression. Five healthy hospital employees, including the hospital administrator, volunteered as control group for the study. Each participant was asked to monitor his or her own symptoms from a checklist of headache, nervousness, dizziness, memory problems, binge eating, lower back pain, nausea, upset stomach, depression, insomnia, uncontrollable temper outburst, or other symptoms.

The hospital's pharmacy prepared 300 mg capsules of aspartame for some participants, and sugar placebos for others. (NutraSweet Company denied the request from the researchers to purchase the aspartame for the study, so the capsules were provided by Schweizerhall, Inc., of New Jersey.) A 154-pound person ingested seven of the prepared capsules daily — the approximate aspartame equivalent would be 10 to 12 cans of diet soda.

Although the study was abbreviated because of the severity of the subjects' symptoms, the researchers did find the incidence of headaches in participants taking aspartame increased and that persons with a history of depression demonstrated significant adverse reactions while taking aspartame. They also reported adverse symptoms for the group taking aspartame increased significantly.[60]

Walton, then chief of psychiatry at New York's Jamestown Hospital and Chautauqua County mental health commissioner, reported a case study of a patient who reacted adversely to aspartame. His 54-year-old female patient "suddenly experienced a grand mal seizure followed by profound behavior changes."

Some of the personality changes included euphoria, flight of ideas, increased motor activity and insomnia. A history of the woman's eating habits revealed she had been accustomed to drinking about a gallon of sugar-

against approval of NutraSweet, saying the Searle tests are unreliable and not adequate to determine the safety of aspartame.[25]

July 15, 1981 Dr. Arthur Hull Hayes, Jr., FDA commissioner, overrules Public Board of Inquiry and approves NutraSweet for dry products saying that aspartame has been shown to be safe for its proposed uses. He says additional evidence, including a third long-term study, assessing aspartame's carcinogenic potential using a different strain of rat confirms that conclusion. The studies he cited were conducted by Ajinomoto, the Japanese manufacturer of aspartame. He says few compounds have withstood such detailed testing and repeated close scrutiny.[5,7,8,26,78]

October 22, 1981 The FDA approves aspartame for table-top sweetener, tablets, cold breakfast cereals, chewing gum, dry bases for beverages, instant coffee and tea, gelatins, puddings, fillings, dairy-product-analog toppings, and flavor enhancer for chewing gum.[27,28]

October 15, 1982 The FDA announces Searle has filed a petition that aspartame be approved as a sweetener in carbonated beverages and other liquids.[6,29]

July 1, 1983 The National Soft Drink Association urges the FDA to delay approval of aspartame for carbonated beverages pending further testing. The FDA responds that it is aware that temperature may affect carbonated liquids containing aspartame, "but believes proper shipping and marketing procedures should 'solve' the problems."[30]

July 8, 1983 Acting commissioner of the FDA, Mark Novitch, approves NutraSweet for use in carbonated beverages and carbonated beverage syrup bases, even though levels of aspartame remaining in beverages stored eight weeks at 68° F were between 84% and 89% of the original amount. "Lost" aspartame degrades to DKP, methanol (methyl alcohol), aspartic acid, and phenylalanine.[31]

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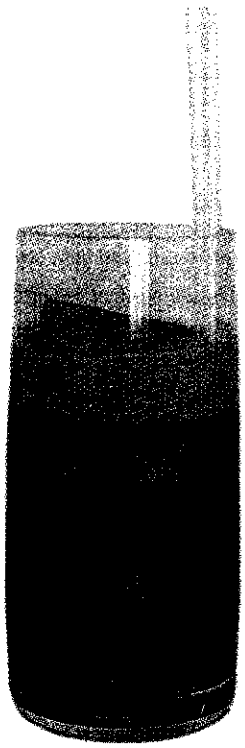
sweetened iced tea daily. In the weeks before her seizure, she had switched from sugar-sweetened tea to an iced tea product containing aspartame. After reviewing her case, Walton advised her to eliminate the aspartame product, upon which she returned to normal and the symptoms subsided.(66)

Walton questions the reliability and validity of studies for the safety of aspartame funded by the NutraSweet Company. "I'm absolutely convinced," he says. "I know it causes seizures. I'm convinced also that it definitely causes behavioral changes. I'm very angry that this substance is on the market. I personally question the reliability and validity of any studies funded by the NutraSweet Company."

In the 1987 proceedings of the First International Meeting on Dietary Phenylalanine and Brain Function, he also presented eight other seizure cases, along with case studies of mania, panic attacks and weight gain induced by aspartame use.

In *No-Nonsense Nutrition For Kids* Annette Natow and Jo Ann Heslin write "animal and human studies have shown that aspartame caused chemical changes in the brain. More research is needed to determine if aspartame is a health hazard."(76)

"I was stunned by the poor quality research and recommended against aspartame's use in carbonated beverages."



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The questions about the validity of the Searle research and tests of aspartame date back to 1976 when FDA was uncertain about the animal test data provided by Searle. The FDA administrators asked Sam Skinner, former U.S. attorney in the Northern District of Illinois, to convene a grand jury to investigate discrepancies in the animal test data provided by Searle. (15)

On January 10, 1977, FDA chief counsel, Richard Merrill, sent a 33-page letter to Skinner repeating the request for the grand jury investigation "into apparent violations of the Federal Food, Drug, and Cosmetic Act ... and False Reports to the Government Act ... by G. D. Searle Company."(12)

The letter also charged that Searle concealed material facts and made false statements in reports of animal studies conducted to establish the safety of the food additive aspartame. The studies cited for investigation had been conducted in 1972, and five-year statutes of limitation for criminal prosecution were due to expire on October 10, and December 8, 1977.(7)

The statutes of limitation ran out before any criminal charges were ever filed. In 1977 Skinner was offered and accepted a job with Sidley and Austin, the law firm that represented Searle. While still U.S. district attorney, Skinner did eventually recuse himself from the Searle investigation. The next U. S. attorney, Tom Sullivan, then dropped NutraSweet from the grand jury investigation.(7)

In 1988 Senator Metzenbaum challenged Skinner's nomination for appointment as U. S. secretary of transportation. Metzenbaum issued a press release that said Skinner "failed to launch a grand jury probe of G.D. Searle, the manufacturer of NutraSweet, which was requested by the Food and Drug Administration. A year after the FDA brought Skinner allegations of fraudulent safety

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July 28, 1983 The National Soft Drink Association drafts an objection to the final ruling, which permits the use of aspartame in carbonated beverages and carbonated beverage syrup bases and requests a hearing on the objections. The association says that Searle has not provided reasonable certainty that aspartame and its degradation products are safe for use in soft drinks. The drafted document is not filed with the FDA. NSDA members feel the case was not strong enough.(32)

August 8, 1983 Consumer attorney James Turner of the Community Nutrition Institute and Dr. Woodrow Monte, Arizona State University's Director of Food Science and Nutritional Laboratories, filed suit with the FDA objecting to aspartame approval based on unresolved safety issues. They request a stay of approval and a public hearing to address aspartame's safety.(6)

September 1983 Searle files an FDA petition for approval of aspartame use in bulk amounts.(33)

September 1983 Commissioner Hayes of the FDA resigns and Burson-Marsteller, Searle's public relation firm hires him as senior scientific consultant. Hayes is unavailable to the press for the next ten years.(19)

Fall 1983 The first carbonated beverages containing aspartame are sold for public consumption.(34)

November 16, 1983 The FDA denies Turner and Monte's request for stay of approval for aspartame use.(35)

December 8, 1983 The FDA proposes to declare aspartame suitable for use as a sweetener in drug products as long as the label warns phenylketonurics that phenylalanine is present.(8)

December 9, 1983 The Arizona Dietetic Association and the Central Arizona District Dietetic Association file a joinder of petition to request a public hearing and

tests by Searle, Skinner took a job with the law firm that defended Searle in the case."[7]

Although Metzenbaum did later say he would not object to the nomination to the position of secretary of transportation, he said that Skinner told him that "he may have made mistakes in his handling the NutraSweet investigation."

The studies under scrutiny were the purview of Dr. Harry Waisman, a researcher at the University of Wisconsin's Regional Primate Center. He was asked to compare toxicity effects from aspartame (particularly seizures and learning defects from brain damage) with those from phenylalanine, a primary ingredient in aspartame.

The FDA and the Centers for Disease Control have received nearly 7,000 complaints regarding aspartame.

Waisman's 52-week toxicity study on seven infant Rhesus monkeys fed a diet containing aspartame did not include a control group for comparison.

The results of the study, submitted to Searle in 1972, showed the death of one monkey after 300 days, the administration of aspartame halted on two monkeys after 200 days, and four monkeys who received aspartame for 365 days. The FDA, in a report on the tests, said that no behavioral or learning tests were undertaken on the monkeys. Former FDA Commissioner Alexander Schmidt, now deceased, said the tests were "shoddy" and "far less than perfect."[79]

A second study initiated by Searle was to have been a 104-week toxicity study on the effects of aspartame on hamsters. The study was halted prematurely after 46 weeks because of an unexpectedly high mortality rate in both control and treated animals following an outbreak of diarrhea among the test animals. Other inconsistencies in the tests were noted upon review by the FDA, including submission of false information, and reports that were written to convey impressions more favorable than underlying data would support.[7,16]

The FDA researchers also said that their agency needed more adequate and better controlled studies. They said the FDA must base its recommendations on sound data because the substance could be part of the daily diet of every American.[25]

Schmidt commented that "if you're approving a food additive that will be taken by children around the world, you will accept absolutely no risk, particularly if it's a non-nutritive sweetener."[7]

The FDA task force observed laboratory methods at Searle from April 25 to August 4, 1977. The Bressler Report (named for team leader Jerome Bressler) identified major discrepancies, including "substantial differences between gross observation on pathology sheets when compared with those submitted to the FDA" in a rat toxicology test of aspartame.[16]

According to the Bressler Report, one rat even appeared resurrected. It stated, "Observed records indicated that animal A23LM was alive at week 88, dead from week 92 to week 104, alive at week 108, and dead at week 112."[16]

The actual meal fed to the rats was

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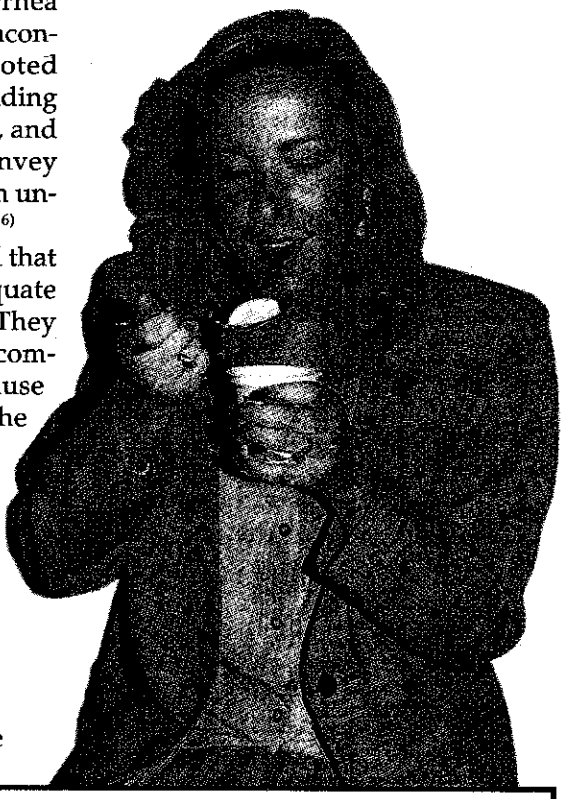

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to add their objections to FDA's approval of aspartame.

December 23, 1983 The Arizona Dietetic Association and the Central Arizona District Dietetic Association file suit in district court seeking an order requiring FDA to hold a hearing. They cite consumer complaints of adverse effects and new medical evidence against aspartame.[6]

February 17, 1984 The FDA denies the request for a public hearing. The district court grants FDA's motion to dismiss the complaint on the ground that "jurisdiction was lacking."[6,36]

March 1984 The FDA and the Centers for Disease Control begin investigations of cases of adverse reactions to aspartame.[7]

May 30, 1984 The FDA approves aspartame for use in multivitamins.[37]

July 10, 1984 Florence Graves, vice-president of publications and editor of *Common Cause* magazine, writes "NutraSweet has been touted as the most tested food additive in history, but our investigation reveals such serious flaws in the government's approval of NutraSweet that Congress should begin its own investigation immediately."[38]

November 1984 The Center for Disease Control reviews 213 of 592 cases of aspartame complaints. Ages of the complainants ranged from four months to 77 years; 77% were between the ages of 21 and 60 years, 75% were female, and 94% were white. Twenty-eight percent reported repeated episodes of symptoms, and 26 people experienced identical symptoms. Some of the reported symptoms included: aggressive behavior, disorientation, hyperactivity, extreme numbness, excitability, memory loss, loss of depth perception, liver impairment, cardiac arrest, seizures, suicidal tendencies, severe mood swings, and death. The CDC recommends future investigations of aspartame investigate the neurological and behavioral problems, and focus on symptoms such

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also in question. Raymond Schroeder, a former Searle employee, said in an FDA interview on July 13, 1977 that "the particles of DKP were large enough to allow the rats to discriminate between the DKP and the basal diet."

In 1982, representatives of the carbonated beverage industry asked Monte to evaluate the scientific data for aspartame. Monte said, "I was stunned by the poor quality research and recommended against aspartame's use in carbonated beverages. I understood that the industry was going to abide by my evaluation but something turned them around."

In 1984, Florence Graves, vice president of *Common Cause* wrote "NutraSweet has been touted as the most tested food additive in history, but our investigation reveals such serious flaws in the government's approval of NutraSweet that Congress should begin its own investigation immediately."[38]

A 1987 report released by the General Accounting Office, "FDA Food Additive Approval Process Followed for Aspartame," included information that waved red flags of potential calamity. Some of the findings in the report:[11]

- The rat DKP Study showed a significant incidence of uterine polyps in rats fed at the two highest dose levels as compared to rats not fed DKP. Review teams later said the polyps were not cancerous, precancerous, or potentially cancerous.
- The Center for Safety and Nutrition advised Searle that because it had not submitted studies for evaluating long-term effects of DKP, as partame was not approved for products that could have an appreciable breakdown to DKP.
- An investigative team report showed that examination of rat fetuses and the reporting of the results in two teratology studies were inadequate.
- Dr. John Olney, psychiatrist, neuropathologist, and professor at Washington University in St. Louis, found 12 brain tumors in 320 dosed rats and none in 120 control rats when he examined FDA files on aspartame animal studies in 1978.
- Olney advised that the high number of brain tumors was unusual.
- Olney voiced another concern based on his research. He showed that when glutamate and aspartic acid are ingested together each agent augments the neurotoxic effects of the other.

Shortly after the U.S. Justice Department's lead prosecutor for the aspartame grand jury investigation was hired by G.D. Searle Company's law firm, the statute of limitations expired and the investigation was dropped.

In a 1981 interview at Washington University Olney said, "Chemicals marketed as food additives are consumed without supervision by hundreds of millions, most of whom do not know they are ingesting the additive, do not derive health benefits from it and have no understanding of its adverse effects."

Olney, along with consumer activist attorney James Turner, initiated court action over aspartame. In a 1986 interview Turner said he had spent 15 years battling approval of aspartame because "it's hurting people."

Monte also called the scientific data supplied on aspartame as "poor quality research" and said he recommended against aspartame's use in carbonated beverages.

Dr. Jeffrey Bada, a chemistry professor at the University of California at San Diego, warned against heating aspartame and the resultant internal rearrangement of its chemical structure.

The late Dr. M. Adrian Gross, an FDA toxicologist, spoke out against aspartame in the August 1, 1985 Congressional Record. Gross, who took part in on-site investigations at Searle

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as headaches, mood alterations, and behavior changes. Frederick L. Trowbridge adds an executive summary to the report which conflicts with the information in the report. He states, "Currently available information, based on data with limitations as described in the report, indicated a wide variety of complaints that are generally of a mild nature. Although it may be that certain individuals have an unusual sensitivity to the product, these data do not provide evidence for the existence of serious, widespread, adverse health consequences to the use of aspartame."[39]

July 17, 1985 An association called "Aspartame Victims and Their Friends" forms.[40]

July 13, 1985 *Editor and Publisher* magazine cites "The Food and Drug Administration NutraSweet cover-up" as one of the most under-reported stories of the year.[44]

August 1, 1985 U.S. Senator Howard Metzenbaum (D-OH) introduces The Aspartame Safety Act of 1985 to Congress.[44]

September 25, 1985 During a visit to the University of Tennessee, then President Ronald Reagan tells a student that he used to carry a vial of sweetener with him but recently quit using sugar substitutes because no one knows what's in them.[43]

October 1, 1985 Monsanto Company purchases G.D. Searle Company, including NutraSweet, for $2.7 billion. Searle's Pharmaceuticals and NutraSweet become separate subsidiaries.[44]

1986 George R. Verrilli, M.D., and Anne Marie Mueser publish *While Waiting: A Prenatal Guidebook*. The book says "aspartame is suspected of causing brain damage in sensitive individuals. A fetus may be at risk for these effects... some researchers have suggested that high doses of aspartame may be associated

laboratories, said the studies carried out by Searle to show the safety of aspartame were "to a large extent unreliable." He said "at least one of those studies has established beyond any reasonable doubt that aspartame is capable of inducing brain tumors in experimental animals and that this ... is of extremely high significance."[42]

Gross also testified that because aspartame was capable of producing brain tumors and brain cancer, FDA should not have been able to set an allowable daily intake of the substance at any level.

He said at least one of Searle's studies "has established beyond any reasonable doubt that aspartame is capable of inducing brain tumors in experimental animals and that this predisposition of it is of extremely high significance....In view of these indications that the cancer causing potential of aspartame is a matter that had been established way beyond any reasonable doubt, one can ask: What is the reason for the apparent refusal by the FDA to invoke for this food additive the so-called Delaney Amendment to the Food, Drug and Cosmetic Act?"

The Delaney Amendment makes it illegal to allow any residues of cancer causing chemicals in foods. In his concluding testimony Gross asked, "Given the [cancer causing potential of aspartame] how would the FDA justify its position that it views a certain amount of aspartame as constituting an allowable daily intake or 'safe' level of it? Is that position in effect not equivalent to setting a 'tolerance' for this food additive and thus a violation of that law? And if the FDA itself elects to violate the law, who is left to protect the health of the public?" ❖

Because of aspartame's potentially hazardous breakdown products, aspartame initially was not intended for use in liquids . . . "It was decided it was too unstable to be used in hot preparations, hot liquids, and also in diet drinks."

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[Editor's Note: Barbara Alexander Mullarkey is an investigative columnist who has been researching aspartame for 12 years. Part Two of this two-part series on aspartame will take a closer look at the medical literature, including what levels of intake are considered dangerous. Future issues of Informed Consent *will also look at safer sweeteners.]*

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13. Letter from Howard J. Trienens, Sidley & Austin, to Samuel K. Skinner, U.S. Attorney, Northern District of Illinois. (January 26, 1977).
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with problems ranging from dizziness and subtle brain changes to mental retardation."[45]

February 3, 1986 Sen. Metzenbaum's investigation reveals that "during a Searle sponsored monkey test, all the animals receiving medium or high dosages of NutraSweet experienced grand mal seizures."[7]

July 17, 1986 Turner files a petition on behalf of the Consumer Nutrition Institute to seek reconsideration of FDA's regulations about safe use of aspartame and to repeal the regulations.[46]

October 16, 1986 Turner files a citizen's petition regarding hazards of seizures and eye damage from aspartame.[27]

November 21, 1986 The FDA denies Turner's petition.[46]

November 28, 1986 The FDA approves aspartame for noncarbonated frozen or refrigerated concentrated and single-strength fruit juice, fruit drinks, fruit flavored drinks, imitation fruit flavored drinks, frozen stick-type confections and novelties, breath mints, and tea beverages.[37]

December 1986 The FDA declares aspartame safe for use as an inactive ingredient provided labeling meets certain specifications.[11]

December 16, 1986 The FDA lists 73 aspartame symptoms, including four deaths, by aspartame complainants.[47]

January 2, 1987 The FDA quarterly report on adverse reactions associated with aspartame states the majority of the complaints by 3,133 individuals refer to neurological effects.[48]

June 18, 1987 The General Accounting Office (GAO) report to Sen. Metzenbaum regarding the approval process for aspartame mentions that 12 of 69 scientists responding to a GAO questionnaire expressed major concerns about aspartame safety, and that during an examination of aspartame animal studies Olney found 12 brain tumors in 320 rats who had received aspartame and that none of the 120 con-

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28. *Federal Register* 46: 50947 (October 16, 1981).

"If you're approving a food additive that will be taken by children around the world, you will accept absolutely no risk."

FDA Commissioner Alexander Schmidt

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trol rats had brain tumors.[11]

August 1987 Mary Stoddard forms the Aspartame Consumer Safety Network in Dallas, Texas.

November 3, 1987 Dr. Jacqueline Verrett, FDA toxicologist and a member of the investigation task force, says the original aspartame studies were "built on a foundation of sand."[20]

February 2, 1988 Four hundred ninety-three U.S. consumer products and 18 over-the-counter pharmaceuticals contain NutraSweet.[49]

February 26, 1988 A letter from David Baine, associate director of the U.S. GAO, states methyl alcohol was not included in the initial description of aspartame because aspartame is only 10% methyl alcohol (by weight).[50]

April 14, 1988 The GAO assignment manager, Michelle L. Roman, admits that some definitions of methyl alcohol define it as a toxic substance.[51]

June 7, 1988 The FDA approves aspartame in yogurt products; frozen desserts; ready-to-serve non-refrigerated, pasteurized, aseptically packaged diluted fruit juice beverages; fruit wine beverages (wine coolers) with ethanol content below seven percent volume; and ready-to-serve gelatin.[37]

October 1, 1988 The FDA quarterly report on adverse reactions associated with aspartame includes 4,204 consumer complaints.[52]

October 19, 1988 The FDA approves aspartame for wafer cookies.[37]

December 21, 1988 Senator Metzenbaum issues a press release saying senators should not approve the appointment of Sam Skinner as Department of Transportation secretary without an inquiry concerning Skinner's failure, as U.S. district attorney in the Northern Illinois District, to pursue allegations about fraudulent testing of NutraSweet. Metzenbaum raises the issue of Skinner accepting a position with Searle's law

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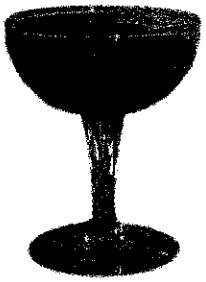

firm, Sidley and Austin, during the time the FDA asked Skinner to review allegations of fraudulent safety tests by Searle and urges the Senate to convene a grand jury to investigate the charges.[53]

January 25, 1989 Senator Metzenbaum issues a press release saying that Skinner acknowledged he may have made mistakes in the NutraSweet investigation, but Metzenbaum says he supports Skinner's nomination as secretary of the Department of Transportation.[54]

June 2, 1989 The FDA approves aspartame for frozen, ready-to-thaw-and-eat cheesecakes; fruit and fruit toppings; and frozen dairy and non-dairy frostings, toppings and fillings.[55]

January 30, 1992 The FDA approves aspartame for malt beverages of less than seven percent ethanol by volume and containing fruit juice; dry, free-flowing sugar substitutes for table use in package unit not exceeding the sweetening equivalent of one pound of sugar; breakfast cereals; and refrigerated ready-to-serve puddings and fillings.[55]

April 16, 1993 The FDA approves aspartame for hard and soft candies.[55]

April 19, 1993 The FDA approves aspartame for all ready-to-serve non-alcoholic flavored beverages, tea beverages, fruit-juice based beverages and their concentrates, baked goods and baking mixes, and as a flavor enhancer in malt beverages containing less than three percent alcohol by volume.[55]

September 17, 1993 The FDA approves additional uses in frostings, toppings, and fillings for baked goods.[55]

February 28, 1994 The Department of Health and Human Services report on adverse reactions attributed to aspartame lists 6,888 complaints, including 649 reported by the Centers for Disease Control, and 1,305 reported by the FDA. Aspartame accounts for the majority (75.7%) of all the complaints in the Adverse Reaction Monitoring System.[56] ❖